MINOT (C. S.)

Dr John Homans
with the compliments of
C. S. Minot

ON CERTAIN PHENOMENA OF GROWING OLD.

ADDRESS

BY

CHARLES SEDGWICK MINOT,

VICE-PRESIDENT, SECTION F,

BEFORE THE

SECTION OF BIOLOGY,

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,

AT THE INDIANAPOLIS MEETING.

AUGUST, 1890.

[From the PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, VOL. XXXIX, 1890.]

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LADIES AND GENTLEMEN :[1]—It is a difficult question to decide what is an appropriate subject for discourse on an occasion like this. It is necessary that it should be at once of a scientific character and of sufficient novelty and originality to fit an occasion of importance, and again, something which is readily understood by an audience of a somewhat miscellaneous range of interests. It would have been, of course, far easier for me to select some one of the special questions which I have been dealing with myself in my more recent study, but rather than do this I have selected a topic more difficult of treatment, to be sure, but at the same time more likely to be profitable and interesting to you. I make this choice because my subject will show that there is a new field, almost unexplored, in the domain of biology into which we are about to enter.

Most of you, I presume, are already familiar with the law of variations as we encounter it in the physical world. Let me offer an illustration, choosing the size of pebbles upon a beach.[2] The size of pebbles is apparently regulated by chance. If a great many of them are measured it is found that there is for a given beach a special size which occurs more frequently than any other. I will represent by a vertical line the number of pebbles of the most frequent size, and by neighboring equidistant lines the number of peb-

bles of other sizes. The diagram, Fig. 1, shows by the height of the lines that the number of pebbles is less the further we go from the most frequent size.

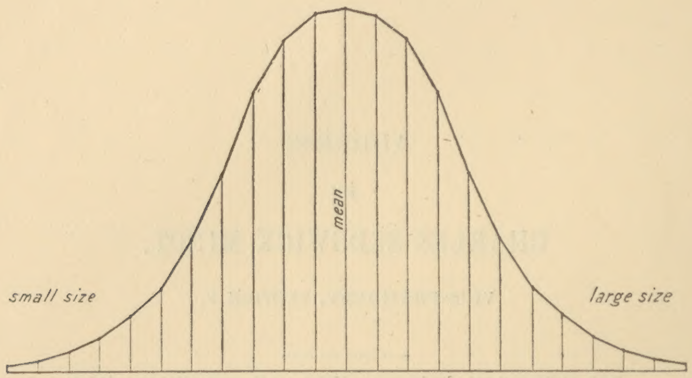

FIG. 1.

This progressive diminution appears equally for the sizes less as well as for those greater than the central size. In other words, the further the departure in size from the most frequent size, the fewer the number of pebbles we find of given dimensions; this is true in like manner of all physical variations. When we connect the tops of all these lines, which represent the number of pebbles, we get a curve which stretches away on each side of the maximum, and when it is drawn accurately and carefully it is found to be strictly symmetrical. This curve goes by the name of the binomial curve, and it is alike on its two sides.

All physical variations, which are produced by the common action of a large and varying number of causes existing in an infinite variety of degrees, present this same peculiarity in the distribution of the variations. When, however, we turn from the physical world to the living world we find that the law of variation is there very different. This can be shown in a great many ways. I have curves here which illustrate this. The first curve which is presented to you is one which is constructed in the same general manner as the one which I sketched for you in regard to the pebbles.

This first curve represents the age of the students who have entered Harvard College during a period of nearly twenty years.[3]

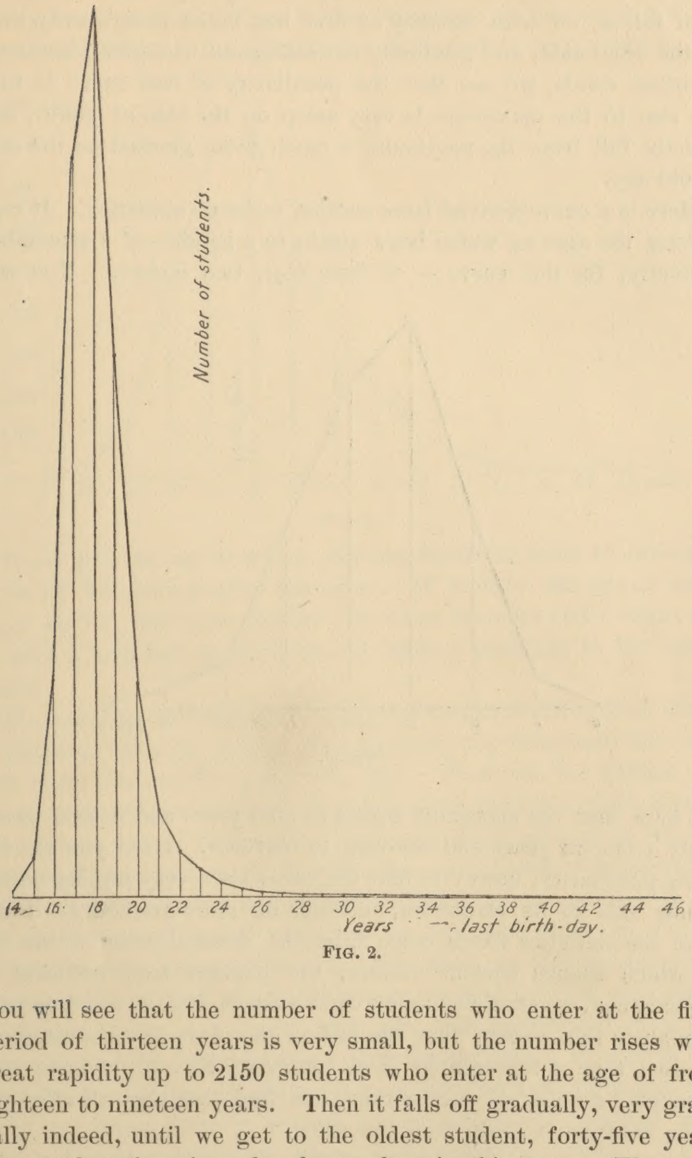

FIG. 2.

You will see that the number of students who enter at the first period of thirteen years is very small, but the number rises with great rapidity up to 2150 students who enter at the age of from eighteen to nineteen years. Then it falls off gradually, very gradually indeed, until we get to the oldest student, forty-five years of age; but there is no break anywhere in this curve. There are no sudden jumps, for the number of observations is so large that the curve becomes quite regular. We notice then that this curve

has the peculiarity of rising with great rapidity to its maximum, then falling off with rapidity at first but much more slowly than on the other side, and gradually extending out to a great distance. In other words, we see that the peculiarity of this curve is that the rise to the maximum is very steep on the side of youth, and that the fall from the maximum is much more gradual on the side of old age.

Here is a curve derived from another series of statistics. It represents the ages at which boys attain to a height—if I remember correctly, for this curve — of four feet, two inches. You will

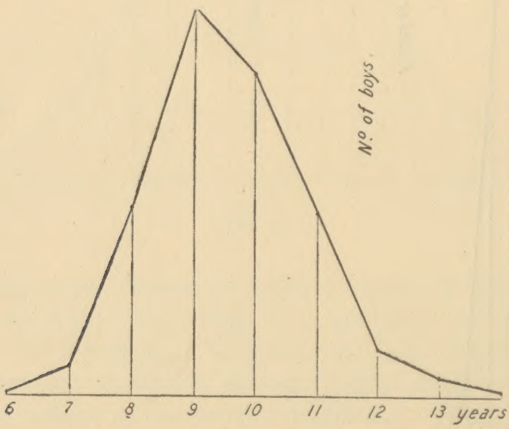

FIG. 3.

see here that the maximum comes at nine years and it rises gradually from six years and extends to fourteen. Here you see the same peculiarity, however, that the curve rises very rapidly on the young side to its maximum, and falls off more gradually. If we take the statistics which come from the determination of the age at which women become mature, the passage from girlhood to womanhood, we shall find that we get a curve, Fig. 4, which is very similar to this, except that the fall on the older side is even more gradual than is represented in the curve of Fig. 3. I have constructed a number of such curves, and find that they all offer the same contrast between their two sides.

Another set of statistics of which, however, I have not constructed curves, is that which gives the relation of the number of children born to the age of the mothers and demonstrates that the

maximum fertility is reached at an age between twenty and twenty-four years, and that the rise to that maximum on the young side is very rapid while on the old side the falling off is very gradual.

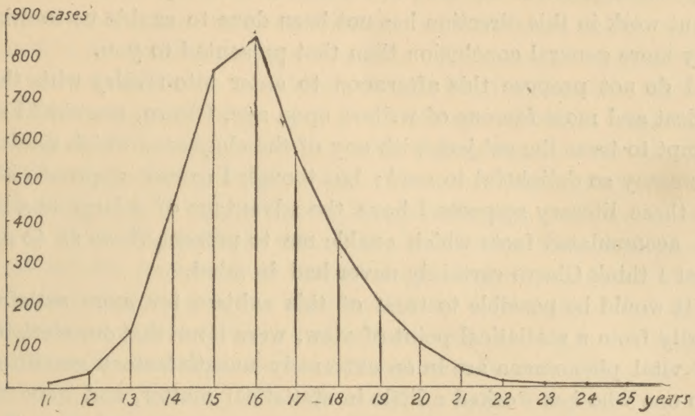

FIG. 4.

If we take the age at which recruits enter the army we obtain a curve of the same general character. If we take the age of marriage we find that also presents the same features and I might go on with a long list of statistics all leading precisely to the same result.

We learn that all curves of biological variation differ from those of physical variation in that, *first*, they are asymmetrical, and, *second*, show this peculiar relation to age. There can be, I think, no question that this alteration which makes the two sides of the curves so unlike is due to that series of changes which goes on in our organs, and which we speak of under the general term of senescence.

I must give warning against generalizing too promptly. In all the above illustrations of variation the maximum occurs at a comparatively early period of life. In other cases, as for instance when we study the relation of suicide to age, we find that the maximum frequency occurs at a much more advanced period and then the curve necessarily becomes steep upon the old side. In fact in the relation of variation to age we have a large field of statistical enquiry, for which there is already a large amount of material that might, if properly put into shape, yield valuable results. From this point of view one might study with profit the relation of various diseases to age, the relation of the birth of first child to the age of the parent, the age of second marriage, the age of entering

the United States senate, the age at which authors have published their first book, the age at which fame has been acquired,[4] etc.,—all these and other similar data might be utilized by the biologist for the investigation of the laws of variation. At the present time sufficient work in this direction has not been done to enable us to draw any more general conclusion than that presented to you.

I do not propose this afternoon to enter into rivalry with that oldest and most famous of writers upon age, Cicero, nor shall I attempt to treat the subject with any of the eloquence which renders his essay so delightful to read; but though I cannot approach him in these literary respects I have the advantage of a large number of accumulated facts which enable me to present views as to age that I think Cicero certainly never had in mind.

It would be possible to treat of this subject far more satisfactorily from a statistical point of view, were it not that our statistics of vital phenomena are in an extremely unsatisfactory condition. To one who has worked a little in statistical matter, and gone far enough to gain some insight into the requirements of that method of research, it is astonishing to find how many elaborate series of statistics have been published which are so erroneous in the manner in which they are presented and the facts grouped that they are nearly valueless for scientific discussion. In order to have any good vital statistics, it is necessary that the exact age of the individual concerning whom the fact is recorded should be known, and that when the data are published they should be put in such form that the facts can be grouped by years; when the variation occurs with very great rapidity, as for instance, in the attainment of maturity in either male or female, it is necessary that the facts should be so published that they may be grouped in months, or even by weeks. These requirements have very rarely been fulfilled.

There could hardly be a better work for a State Board of Health to undertake than the compilation of good vital statistics. We have displayed in this country aptitude for that method of study, as is shown by the superiority of our census returns[5] over those of other countries, and in the accuracy of our army statistics and those of various insurance companies. It seems to me, therefore, that we ought to look to America, where there is so much intelligence, where it is so easily possible to gather facts from the people themselves, for the collection of the best set of vital statistics that have ever yet become available for scientific purposes.

I, myself, have made a series of lengthy experiments intended to give some further insight into the phenomena of senescence.

For several years I had a large colony of Guinea pigs, which I se lected because their period of growth is comparatively short—they attain maturity in something over a year — and it is possible to keep a large number of them, for they are of moderate size, and they have the further advantage that they are easily maintained in the condition of good health. The data of every individual was recorded, its weight at certain fixed ages, etc.; and of those measurements of its growth I have now between eight and nine thousand. In connection with these experiments on the growth, others of a general biological interest were going on, but the whole series of experiments, I regret to say, came to an untimely end. The animals were kept at the Harvard Medical School in one of the rooms of the basement, in large open pens, which gave them ample space for running about. The janitor tied up a bull terrier in the room, but during the night the dog broke loose, and the next morning ninety-six of my animals were lying on the floor shaken to death. Thus the work of nearly five years was in large part swept out of existence, for my experiments depended on their continuance for success. Had it not been for this mishap my results in regard to growth and other problems would have been far more satisfactory than they are now.

The data of the growth of the Guinea pig in weight[6] are, I may venture to say, the most exhaustive series of statistics on the growth of any animal, not even excluding man, which we possess at the present time; they reveal a phenomenon which is illustrated by the chart before you. This chart shows you the percentage of the

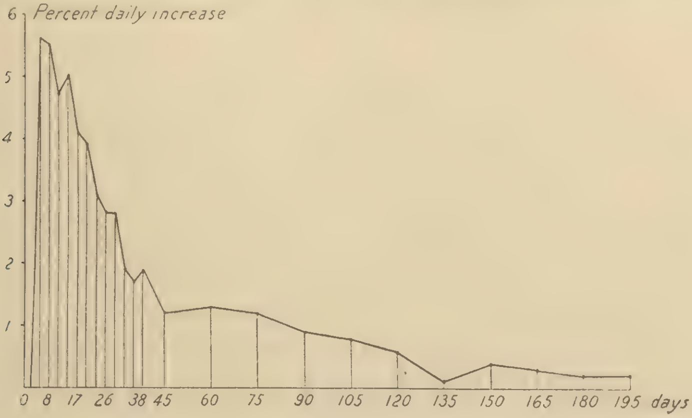

FIG. 5.

weight added to the original weight of the animal during one day's growth. On the left side of the chart the animal is supposed to be young and you notice that the percentage of weight which is added is from five to six. From that period onward to two-hundred and forty-one days, where the data of my experiments stop, there is a steady though slightly irregular fall in the percentage of weight. In other words, when measured by this means, the rate of growth of the Guinea pig declines almost from the moment of birth onward, and there is no such thing in the history of the Guinea pig as a distinction between the period of development and the period of decline. It is one steady decline when we measure the actual growth in this proper, exact manner.

The same law holds true of man, of chickens, of rabbits, of dogs, of ferrets, of all of which animals I possess sufficient statistics to speak with positiveness. In regard to man there are certain fluctuations,[7] to be sure, which occur at about seven, eleven and fourteen years of age, in both sexes, but aside from these variations the progress of the decline is evident from the time of birth to the attainment of the adult size.

The particular curve shown to you, Fig. 5, represents the increase in percentages of males only. Here[8] we have the similar curve of females, and you recognize in the female Guinea pig also, the same progressive loss in power of growth, beginning at a very early period.

I have next another series of charts which illustrates by another means the same phenomenon occurring in the Guinea pig. I have calculated by a simple system of interpolation the length of time required to add ten per cent to the weight of the animal. Now if the animal grows very rapidly it takes but a short time and, as you see, the vertical lines representing those times are very short at the young period, but as the animal grows older the time it takes to add ten per cent to its weight constantly increases. Fig. 6 is the chart of the male Guinea pig, and the similar chart of the female is shown next.[8] From these we learn that whereas the first ten per cent of addition is made in a time a little exceeding two days, the twenty-fifth addition of ten per cent is made in a period of nearly eighty-eight days.

I think the interpretation which we are to give to these facts is, that from the period of birth, which is as far back as observations go at the present time, there is a steady loss of vitality. The notion of development as opposed to decline may perhaps be illustrated

to your minds by comparing it to the construction of a wall by one man. The wall is built and grows larger, develops, but the man grows more and more tired, and as he grows more fatigued, and as

FIG. 6.

the wall becomes higher, the progress thereon becomes slower and slower, but the wall has developed all the while. So we see that the body develops all the time, but the power to continue the development of the body steadily diminishes.

This notion then that there is not from a scientific point of view any distinction to be made between development and decline, is the first generalization which I wish to present to you.

It will be interesting now to turn to the second part of our subject and inquire how far there are any anatomical peculiarities in the organism which can be correlated with this gradual loss of vitality. You will find in the anatomical text books a certain number of peculiarities of the various organs of the body noted as senile character-

istics, as belonging to old age; the change in the shape of the lens of the eye, the induration or ossification of the ligaments and the tendons of the skeleton, and other changes of a like nature, are all carefully put down as characteristic of old age, but it is evident that they belong only to extreme old age, and do not represent or illustrate, so far as we can see at present, any general law or operation going on throughout the entire period of life.

It will be far more instructive for us to turn immediately to the comparison of the youngest with the adult tissues, and to see by close examination what distinctions we can find between the two. In the development of the embryo the germ layers are the first parts to appear. These germ layers are three in number: the outer, the middle and the inner. The outer one forms the external covering of the body; the inner forms the lining of the digestive tract, and the third gives rise in great part to the muscles and connective tissue and skeletal elements of the adult, and the middle portion also gives rise to the blood and the blood vessels. These we may call the primitive parts. Now if we study these three layers as they exist in their primitive form, we observe that at first the cells of the outer layer have each a nucleus, and around that nucleus a small amount of protoplasm which in the chick at least is remarkable for assuming a triangular outline; the nucleus and protoplasm constitute an epidermal cell. When we examine the adult skin of the chick we find that the cells which come there are cells more of this character[9] in which the amount of the protoplasm is very greatly increased. If we examine, in a section of the embryonic intestine, the character of the inner layer cells which form its lining, we shall see that they form a distinct band around the interior of the intestine, and may be represented in this manner. The nuclei are crowded so very closely together, some lying higher, others lower, that the layer seems to consist principally of nuclei. In the adult intestine, we find that the same cells have this characteristic form, an oval nucleus often with a nucleolus; the cell itself is elongated and contains a large amount of protoplasm. If we look at the embryonic connective tissue we see that it presents a similar difference from the adult, for we find a nucleus for each cell, and around that nucleus at first there is merely a tiny layer of protoplasm which sends off its delicate processes in various directions. If we examine the connective tissue corpuscle of the adult, we find that that is a large structure of this character, with a nucleus lying in its inte-

rior, and has very much more protoplasm than does the young cell. This embryonic connective tissue gives rise, however, not only to the connective tissue of the adult, but to various others, cartilage bone, etc.; we find that the cartilage cell in one type occupies a large space with the nucleus surrounded by a considerable amount of protoplasm. The adult bone cell has somewhat of this shape, with an, usually, elongated nucleus, a considerable amount of granular protoplasm and processes running off through the canaliculi of the bone. If we examine the connective tissue cells in the tendon we see that they have this angular form, and are divided up more or less into plates which stick out in an irregular manner and produce this angular outline; we find in them the nucleus lying thus and the amount of protoplasm very much increased indeed. In the case of blood it is even more striking, for we see there that in the youngest blood cells of the bird we have a nucleus with a very distinct outline, and around that nucleus in the youngest blood cells there is merely a fine layer of protoplasm.[10] If we follow the development we find in the latter stages of the embryo that the nucleus has become somewhat smaller and the amount of protoplasm has considerably increased; and in the adult bird we find that the blood corpuscle is oval in shape, large, has a relatively small nucleus and a great deal of protoplasm. We know that similar differentiations recur in the lymph glands, and in the lymph cells.

We have still a second group of tissues, those which arise later in the course of development, and which represent the more specialized organs and tissues of the body. I will consider briefly these in the following order: the nerve cells, the striated muscles, the liver cells, the pancreas cells, the cells of the thyroid and salivary glands, and of the spleen. Sections of the embryonic central nervous system show us that there is at first but one kind of cell. Some of these cells become hardened and form the skeletal portion of the central nervous system. Others undergo progressive development, and become nerve cells, or as they are often called the ganglion cells of the adult. The first trace of the development of these ganglion cells which we can distinguish in the embryo is the enlargement of the nucleus which appears somewhat irregularly granular in this manner. The amount of protoplasm at this time is so small that it is almost indistinguishable around the nucleus. Next the quantity of protoplasm increases. As development progresses the nucleus gradually becomes larger and larger, and in the case at

least of the large motor ganglion cells of the spinal cord becomes large, round, with a distinct nucleolus in the interior, and a slight network running from the nucleolus to the periphery of the nucleus. Around the nucleus, comes a considerable amount of protoplasm, and at the time of birth the proportion of protoplasm to the nucleus, in the case of a ganglion cell, may be represented somewhat as I have sketched it here on the board. From the period of birth to that of adult life the quantity of protoplasm continues increasing and the outline of the cell body becomes finally at least as large in proportion to the nucleus as in this sketch. In the motor ganglion cells we can follow the progressive increase of protoplasm with the greatest distinctness.

In the striated muscle fibre we have a cell which has undergone a peculiar history. It is originally an epithelial cell, but it becomes separated from all its fellows, assumes an elongated form, and the nucleus, which it contained originally, divides so that the elongated cell has several nuclei. The length of the cell goes on increasing for a great while, but the size of the nuclei after they have been once developed does not alter much, and after they have attained their maximum number, which occurs quite early in their development, they do not multiply to any great extent, if at all. Whereas the young muscle fibre may be represented by this outline, the adult muscle fibre has increased to this diameter, and it would stretch so far, if drawn upon the same scale, that its limits would not appear upon this blackboard at all; it would be twenty or thirty times the length of the fibre when it is first differentiated. The enlargement is owing to the growth of the substance of the muscular fibre which has the contractile power, but is the means of locomotion, and is made up of protoplasm. Therefore we have in the striated muscle fibre a striking instance of the increase of protoplasm with age.

In the liver we find the same peculiarity; for the cells with a large nucleus, and but little protoplasm at first, develop into cells with a much larger body in the adult. It is not perhaps worth while to go on repeating these drawings for the pancreas, the thyroid and the salivaries. We can make one general figure for them. The young cell in all of these glands is somewhat of that proportion, and the adult cell is somewhat in the proportion of the sketch of the second figure; and it is the same way in the spleen. You recognize then from this review that in all the principal tissues of the

body we meet everywhere the same phenomenon of growth, namely, that with the increasing development of the organism and its advance in age we find an increase in the amount of protoplasm. We see that there is a certain antithesis, we might almost say a struggle for supremacy, between the nucleus and the protoplasm.

We have then to state as the general result of the studies which we have just made, that the most characteristic peculiarity of advancing age, of increasing development, is the growth of protoplasm; the possession of a large relative quantity of protoplasm is a sign of age.

The facts which we have rested our conclusion upon are drawn, as you have seen, entirely from the study of the vertebrates. It would be easy to show that of a great many of the invertebrates the same law holds; and it is probable that if we had sufficiently exact material to pursue this study throughout the whole animal kingdom down to the cœlenterates, down to the jelly-fish and the polyps, we should find the same law reigning everywhere.

There are many special illustrations of the importance of this relation. I will mention three of these to you. *First*, when the production of a new being takes place, the ovum having been fertilized, the first change which occurs in it is an enormous increase in the amount of nuclear substance, an enormous multiplication of the nuclei in number; the effect of the impregnation of the ovum, of the seed in plants, seems to be an immediate production of nuclear substance; the production of nuclear substance, carried to extreme, converts the ovum after it is fertilized, into a young organism and affords a fresh proof of the fact that the presence of a large amount of nuclear material is characteristic of youth. *Second*, there are certain animals which have the power of producing new parts or of increasing by division. Take, for instance, the class of the common jointed worms which multiply by budding. Here we observe in the middle of the long worm a zone of modified tissue appearing. That zone develops for the front piece of the worm a new tail, and for the hind piece of the worm a new head. The new tail and the new head serve to complete two worms where there was originally but one. The tissue, which does this, is tissue which, before it enters into its developmental accomplishments, assumes the young character, that is, it has a great deal of nuclear substance in proportion to the protoplasm; as it develops into the various tissues attached to the head and tail we see that it differentiates itself by gradual

metamorphoses and by acquiring more protoplasm in its cells. *Third*, take again these same worms which have to a great extent the power of reproducing their lost parts. One may cut off the head or tail of a jointed worm and it will grow again; and this reproduction is always accomplished by means of cells which assume the young character. These three instances teach us that this young character must be considered one of the essential conditions for maintaining a long continued growth.

I regret that my knowledge of botany is so imperfect that I feel in nowise authorized to discuss before you how far the generalization which I have drawn as based upon the study of the animal kingdom can be verified by what occurs among the plants; but I think it can be shown by further study by those who are competent, that the conclusion finds its verification in the vegetable world as well as in the animal. I will venture however to refer to Bütschli's recent investigations,[11] which lead to the conclusion that in bacteria the nucleus is present and very large, while the protoplasm is minimal in amount. This important discovery in conjunction with the extraordinary power of proliferation in bacteria confirms our generalization, that a small proportion of protoplasm is essential to rapid growth.

There are many directions in which investigation might be prosecuted to test this result farther, as for example in the regeneration of the lost arms of star-fishes and of the lost limbs of crabs, and other like instances.

One more fact I will point out before I leave this part of my subject and then I shall reach the general conclusion of my address. There are certain animals which have the power of continuing their growth for a very long period, such, for instance, as the star-fishes and many of the ordinary fishes of the sea; it is curious that we find that in these animals the cells have what I shall call the young character. They contain very little protoplasm.

On the other hand there are certain types which do not grow beyond a definite size and in these, as for instance especially among the insects, we find that the cells are characterized by having a great deal of protoplasm in proportion to the nucleus; so that it seems that everywhere we turn, evidence of a correlation between the growing power and the amount of protoplasm in proportion to the nucleus is encountered.

You perceive the point at which I wish to arrive. I wish to di-

rect your attention to the two sets of phenomena which I have discussed before you this afternoon in conjunction with another. I wish to ask you to consider that there is a progressive loss of vitality going on probably throughout the entire period of life, and that there is farther a relative progressive increase in the amount of protoplasm. The conclusion seems to me inevitable that there is a direct relation of cause and effect between these two phenomena, and I think you will regard me as justified in advancing at least as an hypothesis the belief that the development of protoplasm is the cause of the loss of power of growth. If I were to express the general result which I have to lay before you in the form of an apothegm, I should say that protoplasm was the physical basis of advancing decrepitude. You remember the old definition of protoplasm as the physical basis of life, and undoubtedly there is a certain truth in that; but it is, I think not a little curious to find that by combining the study of the statistician and the histologist we arrive at the somewhat unexpected conclusion—I think I may call it unexpected to you as it was to me—that protoplasm interferes with the power of growth.[12]

It is very unfortunate that this term, the physical basis of life, has been introduced. I suppose every one here has read some of those worthless essays upon protoplasm as the basis of life, wherein it is described as a simple jelly, whereby it is farther proved that protoplasm accounts for everything in a very simple way, that life is very simple and that the writer of the essay perfectly understands it, while it is a complete mystery to every thorough scientific man. I think it an unpardonable wrong for any one to assume that things are so simple when they are so complex, and the real reasoning ought to be that since protoplasm is able to accomplish all the manifold functions of life, and since these functions of life are extremely complex, it follows that protoplasm must have a complexity which is far beyond our present power of conceiving. We know in fact, from the recent investigations which have been made by the improved methods, and by the better lenses which are now at our disposal, that protoplasm has a vast range of complexity which was never dreamed of in the philosophy of those who talk about the simple jelly that explains the cause of life. I beg you all not to think that the half-humorous definition of protoplasm, as the physical basis of advancing decrepitude, expresses the scientific conclusion I wish to lay before you.

There is something else to be learned from the facts that we have had in our minds this afternoon. We have been dealing especially with a series of phenomena which are characteristic of the entire organism and are not confined to any of its organs or system of organs. The zoological part of biology has heretofore consisted almost exclusively of comparative anatomy and of physiology; in other words, in the morphology and physiology of the separate organs of the body. There has been extremely little scientific work done upon the peculiarities of the organism as a whole. It seems to me that in face of the living world we stand very much in the position of a scientific man who should study physics and chemistry in the laboratory and never have the slightest knowledge of geology, or the way in which the physical and chemical forces act in the world and throughout the universe. We should not study merely the organs of the body, whether in their anatomical or their functional relations. There are persons who never understand the arrangement which nature has established. We are always separating the things from their natural connection and taking up a special series of views instead of more general ones. There is in the direction of true *general* biology a vast opportunity which I hope will soon and generously be taken advantage of. There are many things which we can hope to understand only when study is prosecuted from that point of view. All of the important phenomena of reproduction, of heredity, of the evolution of species and of all the relations of actual organisms to the general economy of nature, of sex, of growth and variation, even of death itself, which is a problem I believe capable of scientific solution;— all these things are hidden away to a large extent from the morphologist and physiologist: they are open to the general biologist, and we recognize immediately when it is laid before us for careful consideration, that here is a great and unexplored field lying open to all those who have the patience and diligence to work in it. The results will be great. But something more than scientific enthusiasm and scientific capacity is needed for the prosecution of this kind of work. To carry it on properly large numbers of animals and plants must be kept under specific conditions for considerable periods of time — as you know, a costly undertaking; and if you will consider but a moment the small wealth of scientific men, I think you will feel that there are very few who out of their private means can enter upon such researches and undertake

these experiments. But beside those who pursue science as their professional work, there are many who have large means and generous impulses, and who have a real interest in science and a genuine desire to assist it. We see in the numerous institutions which are founded on every hand, in the endowments given to colleges, to libraries, to museums and to various public institutions, the proof that there is a most liberal and noble spirit on the part of men who take no active share in the work of science, leading them to do all that lies in their power to assist it. I hope among those who feel such impulses there may be some who will recognize that there is a new field open to them in which they may coöperate. There is an abundant crop of facts to be gathered. Zeal is there to harvest it and I hope that which is necessary to supplement zeal and ability, the wherewithal to carry out their purpose, may not be lacking.

I speak thus particularly of the advantage of the endowment of research in this way because I have had personal experience of the degree to which it is important. There has been intrusted to my care a fund which yields an income of something over a thousand dollars, which is appropriated exclusively to the endowment of research.. Grants are made to meet the cost of investigations, which otherwise could not be carried out. Last year over twenty thousand dollars were applied for, and if we could have given fifteen thousand in response to deserving applications from men of acknowledged standing, the amount would have been wisely bestowed and have been worthily and properly used to the advantage of science. Such an experience has taught me that there is a greater store of scientific enthusiasm and capacity waiting for opportunities and means, than we have ever recognized. No other proof is wanted that the great need of science to-day is the endowment of research. I rejoice that this Association applauded so generously as it did the announcement made this morning that an addition, though not of very great amount, had been made to the small research fund of the Association. I think that nothing could more nobly commemorate a meeting of this Association than such a gift as came to us from Toronto. After this there will exist in the Association a permanent record of the hospitality and generosity of our Toronto hosts, and they will feel that they continue through us to contribute toward the direct promotion of science.

Wherever we turn we see scientific work of the highest quality delayed and even stopped for the lack of means. Everyone who can rescue these opportunities from being lost, even in part, will deserve well of mankind and deserve the acknowledgments of this Association.

NOTES.

[1] The address is given nearly as delivered. The changes have been confined to verbal alterations, except in the reference to the nucleus of bacteria, which is a subsequent addition, and in the closing paragraph, where the changes amount to rewriting the stenographic report.

[2] It would perhaps have been better to choose an illustration for which actual figures could be presented. I did, however, collect and weigh several years ago a considerable number of pebbles from a beach at Salem, Massachusetts, taking *all* pebbles I could find on the surface of a small area and obtained a symmetrical though somewhat jagged binomial curve. I regret now that I did not preserve the figures.

[3] For the data concerning the students entering Harvard College I am indebted to the kindness of President C. W. Eliot, to whom I take this opportunity to express my thanks. The table on the next page gives the ages in detail.

[4] A curious study of this subject, the Age of Fame, has been published by Mr. Elliott in the International Review.

[5] This was written before the disgraceful inaccuracy of the census of 1890 was known.

[6] The detailed memoir upon the growth of Guinea pigs, is now in press and will appear in the Journal of Physiology.

[7] These fluctuations are best shown in the tables of growth published by Dr. H. P. Bowditch in the Annual Report of the Massachusetts State Board of Health for 1873.

[8] The curve referred to is omitted. It may be found in the memoir mentioned in Note 6.

[9] The appearances described were sketched upon the blackboard; as they are figured in the text books of embryology, histology and anatomy, it has been deemed unnecessary to add illustrations to the text.

[10] The amount of protoplasm in the youngest blood cells is so small that some writers have overlooked it and erroneously held that the blood corpuscles arose as nuclei.

[11] O. Bütschli, Ueber den Bau der Bacterien, 1890.

[12] This law will perhaps give the clew to the intimate relation between the hypertrophy and degeneration and necrosis of cells. This relation is familiar to pathologists.

YEAR.	14–15	15–16	16–17	17–18	18–19	19–20	20–21	21–22	22–23	23–24	24–25	25–26	26–27	27–28	28–29	29–30	30–31	31–32	32–33	45–46	AVERAGE AGE.	NO. ADMITTED.
1856	4	16	44	34	29	7	1	4		3		2										144
1857		6	31	27	25	8	3	3		5												108
1858		7	23	43	30	11	3	2	2	3												124
1859		6	26	56	31	14	5	3	1	1	1											144
1860		9	26	38	33	14	9	1	4	2												136
1861		3	24	50	23	13	3	5	1	2			1		1							126
1862		2	19	41	30	15	10	3	2				1									123
1863	1	2	22	38	36	13	5	7		2			1		1							128
1864	1		14	30	18	19	6	3	1		1				1	1						97
1865		5	19	51	28	23	9	1	5		1		1									143
1866		6	19	38	46	23	8		3	1												144
1867			22	56	55	24	7	9	3	1	1											178
1868			16	48	37	22	13	2	1	2												141
1869		2	15	49	52	22	11	6						1	1							159
1870		3	19	76	53	29	11	4	4	1	1			1								203
1871		6	24	59	62	28	16	4	1	1												201
1872		2	20	51	65	29	12	4	2	1				1								188
1873	1	2	19	52	76	43	17	11	3	4	2	5		1								236
1874	1	2	19	61	58	42	7	4	1	2	2	2		1								202
1875	1	1	12	78	93	49	10	7	3	4												258
1876		1	12	58	60	53	20	7	2	2	1		1									217
1877		2	16	52	80	53	23	9	6	3	1											245
1878		2	14	52	78	45	22	7	9		1											230
1879		1	16	49	86	53	19	15	4	1	1	1	1	1								248
1880		1	12	52	84	53	24	9	3	4	1	2	1	1								247
1881		3	10	38	73	55	31	10	8	1	1											230
1882	1	3	11	58	89	60	28	12	4	5	1	2						1				275
1883			17	65	100	61	23	7	7	2	2	1										285
1884	1		12	63	99	72	29	8	4	1	5	1										286
1885	2		10	63	89	56	40	6	4	4	1	2				1	1		1	1		281
1886		4	14	64	116	67	29	12	3	3	2	1		2			2					321
1887			8	66	102	81	23	5	5	1	2	1	2				1					296
1888			13	56	114	63	27	12	4	2	3		1	1								296
1889		1	14	61	109	79	21	4	3	1	3	1	1	1	1				1			300
Totals.	13	98	522	1775	2150	1299	514	206	103	67	34	22	11	11	5	2	4	1	2	1		6840